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Supreme Court, U.S.
FILED
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No. 06-1498

IN THE

Supreme Court of the United States

WARNER-LAMBERT COMPANY LLC AND PFIZER INC.,
Petitioners,

v.

KIMBERLY KENT, *et al.*,
Respondents.

On Writ of Certiorari to the United States Court of Appeals for the Second Circuit

BRIEF OF PETITIONERS

DAVID KLINGSBERG
STEVEN GLICKSTEIN
KAYE SCHOLER LLP
425 Park Avenue
New York, N.Y. 10022
(212) 836-8000

CARTER G. PHILLIPS*
DANIEL E. TROY
REBECCA K. WOOD
EAMON P. JOYCE
QUIN M. SORENSON
SIDLEY AUSTIN LLP
1501 K Street, NW
Washington, D.C. 20005
(202) 736-8000

Counsel for Petitioners

November 21, 2007 * Counsel of Record

WILSON-EPES PRINTING CO., INC. – (202) 789-0096 – WASHINGTON, D. C. 20002

QUESTION PRESENTED

Michigan law shields manufacturers from product liability claims with respect to prescription drugs approved by the United States Food and Drug Administration ("FDA"). See Mich. Comp. Laws § 600.2946(5). This protection does not apply, however, and thus a claim may proceed if the fact-finder determines that the manufacturer-defendant:

> Intentionally withholds from or misrepresents to [FDA] information concerning the drug that is required to be submitted under the federal food, drug, and cosmetic act, chapter 675, 52 Stat. 1040, 21 U.S.C. 301 to 321, 331 to 343-2, 344 to 346a, 347, 348 to 353, 355 to 360, 360b to 376, and 378 to 395, and the drug would not have been approved, or [FDA] would have withdrawn approval for the drug if the information were accurately submitted.

Id. § 600.2946(5)(a).

Question presented:

Whether, under the implied preemption principles of *Buckman Co.* v. *Plaintiffs' Legal Committee*, 531 U.S. 341 (2001), federal law preempts state law to the extent it permits or requires a fact-finder to speculate as to whether a defendant improperly disclosed information to the federal agency that materially affected the agency's decision to approve or not withdraw the drug.

PARTIES TO THE PROCEEDING

Petitioners, defendants-appellees below, are Warner-Lambert Company LLC and Pfizer Inc.

Warner-Lambert Company LLC is wholly owned by Pfizer Inc. Pfizer Inc. has no parent company, and no privately held company owns 10 percent or more of its stock.

Respondents, plaintiffs-appellants below, are the following 27 individuals:

Kimberly Kent, Personal Representative of the Estate of Virginia Kent

Emmett Kent

Connie Armstrong

Lauranane Bradley

Raymond Bradley, Sr.

Glenn Chandler

Billie Jo Flynt

Shelly Grotenhius

Judy Ann Hearn

Colleen Rose Herndon

Michael Herndon

Michael H. Kanakry

Mary Ann Kanakry

Julia Lynne Martin

Royal M. Martin

Janice L. Kimmel, Personal Representative of the Estate of Thea Martz

Mona Lorene Przytulski

David A. Rice, Personal Representative of the Estate of Robert Rice

Anita Louise Schultz

Richard P. Schultz

James Soukup, Personal Representative of the Estate of Barbara Soukup

Jennifer St. Pierre, Personal Representative of the Estate of Raymond St. Pierre

Donald R. Waun

Jean Waun

Linda Sherman

Stanley Sherman

Nancy Fisher, Individually and as Personal Representative of the Estate of Troy Fisher*

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* Elizabeth M. Graham and Robert C. Graham, respondents at the time the petition for certiorari was filed, have since voluntarily dismissed their case. See *Graham* v. *Warner-Lambert*, Stipulation And Order Of Dismissal With Prejudice, No. 00cv2843 (LAK), Doc. No. 4779 (S.D.N.Y. ordered July 13, 2007; entered July 16, 2007).

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CDER, FDA, *CDER Handbook* (1998), *available at* http://www.fda.gov/cder/handbook/handbook.pdf 6

CDER, FDA, *Meeting Number 74 of: Endocrinologic & Metabolic Drugs Advisory Committee ("EMDAC")* (May 19, 2000), *available at* http://www.fda.gov/ohrms/dockets/ac/00/transcripts/3615t1.pdf 13, 14, 15

FDA, *Fast Track, Accelerated Approval and Priority Review* (May 2006), *at* http://www.fda.gov/oashi/fast.html 13

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OPINIONS BELOW

The order of the court of appeals denying Warner-Lambert Company LLC and Pfizer Inc.'s petition for rehearing and for rehearing en banc was entered on February 12, 2007, is unreported, and is reprinted in the appendix to the petition for certiorari ("Pet. App.") at 39a-40a. The underlying order of the court of appeals was issued on October 5, 2006; an amended opinion was entered on January 18, 2007, is reported at 467 F.3d 85 (2d Cir. 2007), and is reproduced at Pet. App. 1a-28a. The order of the United States District Court for the Southern District of New York, and the transcript in which the district court set forth its reasoning, were entered on February 24, 2005, are unreported, and are reprinted at Pet. App. at 29a-38a.

JURISDICTION

The initial opinion of the court of appeals issued on October 5, 2006, and on January 18, 2007, the court entered an amended opinion modifying its decision. On February 12, 2007, the court of appeals denied rehearing. The petition for a writ of certiorari was filed on May 10, 2007, and was granted on September 25, 2007. JA 47-48. This Court has jurisdiction pursuant to 28 U.S.C. § 1254(1). Notification has been made under Rules 14.1(e)(v) and 29.4(c) of the Rules of this Court.

RELEVANT CONSTITUTIONAL, STATUTORY, AND REGULATORY PROVISIONS

The Supremacy Clause of the United States Constitution provides in pertinent part that "the Laws of the United States . . . shall be the supreme Law of the Land . . . any Thing in the Constitution or

Laws of any State to the Contrary notwithstanding." U.S. Const. art. VI, cl. 2.

Provisions of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301 *et seq.* ("FDCA") expressly invoked by the Michigan provision are 21 U.S.C. §§ 301 to 321, 331 to 343-2, 344 to 346a, 347, 348 to 353, 355 to 360, 360b to 376, and 378 to 395. Section 337(a) provides in relevant part that "all ... proceedings for the enforcement, or to restrain violations, of this chapter shall be by and in the name of the United States." 21 U.S.C. § 337(a). The text of the remaining pertinent provisions (*id.* §§ 332, 333, 334, 336, 337, 355, 372, 375(b), 393) is set forth in the Pet. App. at 43a-130a, or in the appendix hereto at 1a.

Pertinent regulations are Sections 10.30, 20.1, 314.50, 314.80, 314.81, 314.105, 314,125, and 314.150 of chapter 21 of the United States Code of Federal Regulation. The pertinent text of these provisions is set forth in the Pet. App. at 131a-192a, or in the appendix hereto at 2a-6a.

The pertinent provision of the Michigan statute in question, Mich. Comp. Laws § 600.2946(5), is set forth in the Pet. App. at 42a.

STATEMENT OF THE CASE

The Second Circuit's decision cannot be reconciled with this Court's holding in *Buckman Co.* v. *Plaintiffs' Legal Committee*, 531 U.S. 341 (2001). In *Buckman*, this Court held that federal law impliedly preempts plaintiffs' claims that a manufacturer was liable under state law for alleged misrepresentations made to FDA in violation of federal regulatory obligations governing the approval of medical products for marketing in the United States. *Id.* at

348. As this Court held, "[s]tate-law fraud-on-the-FDA claims inevitably conflict with the FDA's responsibility to police fraud consistently with the Administration's judgment and objectives." *Id.* at 350. Permitting a trier-of-fact to determine whether a manufacturer violated federally imposed duties to the agency—a relationship "inherently federal in character"—could not be squared with the role Congress delegated to FDA alone. *Id.* at 347-48.

Under the state-law provision at issue here, before a plaintiff's claims can be adjudicated, a fact-finder must determine that the manufacturer (i) "withh[eld] from or misrepresent[ed] to [FDA] information"; (ii) that was "required to be submitted under" the provisions of the federal statute FDA administers; and (iii) that the agency "would have withdrawn approval for the drug if the information were accurately submitted." Mich. Comp. Laws § 600.2946(5)(a). Thus, the provision at issue here, like the claims in *Buckman*, impermissibly requires a trier-of-fact to intrude upon an exclusively federal domain and to decide matters that inevitably conflict with FDA's authority to police fraud-on-the-agency. As such, the provision is preempted; the Second Circuit's judgment should be reversed; the judgment of the district court should be restored and respondents' claims should be dismissed with prejudice.

A. Statutory Background

1. *Federal regulation of prescription drugs in the United States.* For more than a century, since the Pure Food and Drug Act of 1906, Congress has charged FDA, and its predecessor agencies, with regulating drugs in the United States. See generally John P. Swann, *History of the FDA*, *at* http://www.fda.gov/oc/history/historyoffda/default.htm. FDA's

responsibility has increased over time. In 1938, the Federal Food, Drug, and Cosmetic Act ("FDCA"), Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301 *et seq.*), enhanced FDA's authority, and required "that an application be submitted to the FDA before any 'new drug' [could] be introduced into interstate commerce." *United States* v. *Generix Drug Corp.*, 460 U.S. 453, 458 (1983). The Drug Amendments of 1962 empowered FDA to evaluate not only safety, but also effectiveness. See Pub. L. No. 87-781, 76 Stat. 780 (1962).

At "[t]he heart" of the FDCA "is the grant of primary jurisdiction to FDA, the expert agency [Congress] created." *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 627 (1973). One of the FDCA's "core objectives is to ensure that any product regulated by the FDA is 'safe' and 'effective' for its intended use." *FDA* v. *Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000); see 21 U.S.C. § 393(b)(2)(B). To this end, Congress charged FDA with "promot[ing] the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner." 21 U.S.C. § 393(b)(1). In making its determinations, FDA imposes a "strict and demanding" review. *Hynson*, 412 U.S. at 619.

Before a prescription drug can be marketed in the United States, the manufacturer typically must submit a New Drug Application ("NDA") to FDA that scientifically demonstrates the safety and efficacy of the drug for its intended use. See 21 U.S.C. § 355(b); 21 C.F.R. § 314.50 (detailing form and content of NDA). In this process, the FDCA and its regulations impose detailed federal disclosure obligations from the manufacturer to the agency. An NDA therefore must contain "full reports of investigations"

supporting safety and effectiveness, as well as submissions regarding the drug's components and composition; methods and controls used in manufacturing, processing, and packing the drug; and specimens of the warning labeling proposed to be used for the drug. 21 U.S.C. § 355(b)(1)(A)-(F). Federal law further requires the applicant to submit, and FDA to review, extensive analyses of clinical studies, pharmacological action, and toxicological effects of the drug. See 21 C.F.R. § 314.50(d).

Given the breadth of these requirements, a typical NDA spans many thousands of pages and is grounded in clinical trials that are conducted over many years.[1] In reviewing this extensive information, "FDA is required to exercise its scientific judgment to determine the kind and quantity of data and information an applicant is required to provide for a particular drug to meet the statutory standards." *Id.* § 314.105(c). To that end, FDA reviews the NDA and ascertains whether it complies with federal disclosure requirements—and whether safety and efficacy have been proven to the agency's satisfaction. See generally 21 U.S.C. § 355(d) (grounds for denying NDA); 21 C.F.R. § 314.125 (same).

FDA typically spends well over a year evaluating NDA submissions and approves fewer than 100

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[1] *See, e.g.*, *Citizens Comm'n on Human Rights* v. *FDA*, 45 F.3d 1325, 1327 & n.4 (9th Cir. 1995) (NDA file of 300,000-400,000 pages); *Merix Pharm. Corp.* v. *GlaxoSmithKline Consumer Healthcare, L.P.*, No. 05 C 1403, 2006 WL 2931260, at *5 (N.D. Ill. Oct. 11, 2006) (NDA file of 175,000 pages); GAO, *New Drug Development, Report to Congressional Committees*, 26 Biotech. L. Rep. 82, app. 1 at 94 (2007) (underlying clinical trials average seven years to complete successfully).

NDAs a year.[2] The agency conducts a "comprehensive scientific evaluation of the product's risks and benefits under the conditions of use," not an "abstract" assessment. FDA, Requirements on Content and Format of Labeling for Human Prescription Drugs and Biological Products, 71 Fed. Reg. 3922, 3934 (Jan. 24, 2006).[3] During this time, FDA communicates with the company about "scientific, medical, and procedural issues that arise during the review process," ranging from "easily correctable deficiencies," to a "need for more data or information, or for technical changes," to "major scientific issues" that must be addressed before moving forward. See Ctr. for Drug Evaluation & Research ("CDER"), FDA, *CDER Handbook* 24 (1998), *available at* http://www.fda.gov/cder/handbook/handbook.pdf; see *id.* at 19 (chart of NDA review process).

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[2] *See* GAO, *supra*, at 86 (FDA took an average of 442 days to approve an NDA in 2002); CDER, FDA, *CDER Approval Times for Priority and Standard NDAs and BLAs Calendar Years 1993-2006* (2007), *available at* http://www.fda.gov/cder/rdmt/NDAapps93-06.htm (FDA approved 101 NDAs and "BLAs" (a similar process for biological products) in 2006: 21 priority track and 80 standard track; FDA approved 80 total in 2005); FDA, *New Drug Application Approvals and Receipts, Including New Molecular Entities, 1938 to Present*, *available at* http://www.fda.gov/oc/history/NDAapprovals.html (approving 22 new molecular entities in 2006, and 20 in 2005).

[3] *See* 21 C.F.R. § 314.50(d)(5)(viii) (NDA requires a "summary of the benefits and risks of the drug, including a discussion of why the benefits exceed the risks *under the conditions stated* in the labeling") (emphasis added); *United States* v. *Rutherford*, 442 U.S. 544, 556-57 (1979) (recognizing that the balance between drug effectiveness and safety for approved drugs will vary depending on the condition for which medication is indicated).

Following its review, "FDA will approve an application after it determines that the drug meets the statutory standards for safety and effectiveness, manufacturing and controls, and labeling." 21 C.F.R. § 314.105(c); see *id.* §§ 201.56(d), 201.57. Conversely, FDA "shall issue an order refusing to approve" the NDA if, in FDA's judgment, the submissions from the manufacturer "do not include adequate tests"; "the results of such tests show that such drug is unsafe for use" or "do not show that such drug is safe for use"; "there is a lack of substantial evidence that the drug will have the effect it purports"; or if the labeling "is false or misleading in any particular." 21 U.S.C. § 355(d). The agency may deny approval for a number of other reasons, including if FDA were to determine that the NDA "contains an untrue statement of a material fact." 21 C.F.R. § 314.125(b)(7).[4]

After approval, FDA continues to monitor approved drugs closely. See generally 21 U.S.C. § 355(k) (imposing postmarketing recordkeeping and reporting requirements on the manufacturer). For instance, the manufacturer must review and timely report to FDA "[a]ny adverse event associated with

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[4] FDA also may deny approval if, *inter alia*, it determines the methods and controls for the manufacturing, processing, and packing of the drug are inadequate to preserve its strength, quality, purity, and stability; the investigations "do not include adequate tests" to "show whether or not the drug is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling"; "[t]he results of the tests show that the drug is unsafe for use under the conditions prescribed, recommended, or suggested in its proposed labeling or the results do not show that the drug product is safe for use under those conditions"; or "insufficient information about the drug" exists to determine whether it is "safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling." 21 C.F.R. § 314.125(b).

the use of a drug in humans, whether or not considered drug related," including events "occurring in the course of the use of a drug product in professional practice" and from overdose, abuse or withdrawal, as well as "any failure of expected pharmacological action." 21 C.F.R. § 314.80(a)-(c). The manufacturer must submit annual reports notifying the agency of any "significant new information ... that might affect the safety, effectiveness, or labeling of the drug," new clinical data, nonclinical laboratory studies, and status reports on postmarketing studies. See *id.* § 314.81(b)(2). Those reports must include scientific literature and postmarketing studies. *Id.* § 314.80(d)-(e). FDA also has informal mechanisms for assessing and reacting to postmarketing information. See generally Michelle Meadows, *Why Drugs Get Pulled Off the Market*, FDA Consumer, Jan.-Feb. 2002, *available at* http://www.fda.gov/fdac/features/2002/102_drug.html (discussing several examples of the agency's reaction to postmarketing information).

Congress recently further enhanced FDA's postmarketing powers in the Food and Drug Administration Amendments Act of 2007 ("FDAAA").[5] FDAAA grants FDA authority to require, *inter alia*, (i) additional post-approval studies or clinical trials, and (ii) new safety labeling changes on an expedited basis. Pub. L. No. 110-85, § 901, 121 Stat. 823, 922-43; see FDA, *Law Strengthens FDA*, *available at* http://www.fda.gov/oc/initiatives/advance/fdaaa.html ("This new law represents a very significant addition

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[5] *See* Pub. L. No. 110-85, 121 Stat. 823, 823 (2007) ("An Act to amend the [FDCA] ... to enhance the postmarket authorities of the [FDA] with respect to the safety of drugs, and for other purposes."); *id.* § 909, 121 Stat. at 950 (FDAAA "takes effect 180 days after the date of the enactment," *i.e.*, September 27, 2007).

to FDA authority."). FDAAA also, for example, expands a clinical trial data bank to make detailed information regarding the design, conduct, and results of drug trials publicly available through the Internet. See Pub. L. No. 110-85, § 801, 121 Stat. at 904-22. It further establishes an Advisory Committee on Risk Communication, "composed of experts on risk communication" as well as "representatives of patient, consumer, and health professional organizations" to facilitate disclosure of risk information. *Id.* § 917, 121 Stat. at 960.

In its review of postmarketing information, FDA "shall . . . withdraw approval" of a previously approved drug if the agency determines, among other things, that "scientific data show that such drug is unsafe for use" under the conditions of approval. 21 U.S.C. § 355(e). In addition, FDA may find withdrawal necessary if it determines, *inter alia*, that the company has "deliberately failed to maintain required records or to make required reports" under FDA standards; failed to explain the omission of certain information in agency submissions; or failed to comply with FDA standards in an "essential" study underlying the NDA such that the "validity of the study" is called into doubt. 21 C.F.R. § 314.150(b)(1), (6), (7).

In applying these standards, under the FDCA, "it is the Federal Government rather than private litigants who are authorized to file suit for noncompliance" with the FDCA or its regulations. *Buckman*, 531 U.S. at 349 n.4; see *Thompson* v. *Western States Med. Ctr.*, 535 U.S. 357, 362 (2002) ("The FDCA invests [FDA] with the power to enforce its requirements."). Indeed, Section 337(a) expressly provides that "all . . . proceedings for the enforcement, or to restrain

violations, of this chapter shall be by and in the name of the United States." 21 U.S.C. § 337(a).

In exercising its enforcement prerogatives, FDA may examine drugs and investigate suspected fraud or misrepresentations by the manufacturer. *Id.* § 372. Should FDA find a problem, it has a range of options, including *in rem* forfeiture, injunction, and criminal prosecution against the responsible party if a "misbranded" drug is distributed in the United States market. See *id.* § 332(a) (injunctions); *id.* § 333 (criminal penalties); *id.* § 334(a) (seizure); and *id.* § 337(a) (enforcement proceedings); *Merrell Dow Pharms. Inc.* v. *Thompson*, 478 U.S. 804, 810-12 (1986); *id.* at 830 (Brennan, J., dissenting) ("Congress has provided the FDA with a wide-ranging arsenal of weapons to combat violations of the FDCA"). FDA has brought a number of enforcement actions in recent years and negotiated consent decrees that include disgorgement provisions ranging from $30-$500 million. See *United States* v. *Lane Labs-USA Inc.*, 427 F.3d 219, 234 (3d Cir. 2005) (citing examples).

Congress also has provided FDA with express statutory discretion to impose less stringent measures where the agency deems it appropriate. See 21 U.S.C. § 336 ("Nothing in [FDCA] shall be construed as requiring [FDA] to report for prosecution, or for the institution of libel or injunction proceedings, minor violations of this chapter whenever [FDA] believes that the public interest will be adequately served by a suitable written notice or warning.").[6] This Court has recognized that FDA has

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[6] *See also* 21 U.S.C. § 375(b) (FDA may "disseminate[] information . . . in situations involving, in the opinion of the Secretary, imminent danger to health or gross deception of the

unreviewable discretion to decide how best to enforce the FDCA. See *Heckler* v. *Chaney*, 470 U.S. 821, 837-38 (1985) (FDA's decision not to take enforcement action is not subject to judicial review); see also *Brown & Williamson*, 529 U.S. at 181 (Breyer, J., dissenting) (FDCA should be interpreted in a manner that "both permits the FDA to take into account the realities of human behavior and allows it, in appropriate cases, to choose from its arsenal of statutory remedies").

FDA's regulations also provide a vehicle for citizens to report alleged violations, including fraud, to FDA and petition the agency to take regulatory or enforcement action. See 21 C.F.R. § 10.30 (allowing citizens to request that the agency "issue, amend, or revoke a regulation or order or take or refrain from taking any other form of administrative action"); *Buckman*, 531 U.S. at 349.

2. *The Michigan Statute.* As part of state-law tort reform, the State of Michigan enacted legislation providing that:

> In a product liability action against a manufacturer or seller, a product that is a drug is not defective or unreasonably dangerous, and the manufacturer or seller is not liable, if the drug was approved for safety and efficacy by the [FDA], and the drug and its labeling were in compliance with the [FDA's] approval at the time the drug left the control of the manufacturer or seller.

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consumer" and "collect[], report[], and illustrat[e] the results of the investigations of the Department"); Ernest Gellhorn, *Adverse Publicity by Administrative Agencies*, 86 Harv. L. Rev. 1380, 1408 (1973) (oftentimes "FDA ensures compliance by threatening seizure, injunction, and the issuance of publicity"; "publicity is usually the most potent persuader").

Mich. Comp. Laws § 600.2946(5); Pet. App. 3a.

At issue here is a companion provision of the Michigan statute withdrawing this defense if a plaintiff proves to the fact-finder that the manufacturer "[i]ntentionally withholds from or misrepresents to [FDA] information concerning the drug that is required to be submitted under the [FDCA]"—expressly invoking the provisions discussed above, see 21 U.S.C. §§ 301 to 321, 331 to 343-2, 344 to 346a, 347, 348 to 353, 355 to 360, 360b to 376, and 378 to 395—"and the drug would not have been approved, or [FDA] would have withdrawn approval for the drug if the information were accurately submitted." Mich. Comp. Laws § 600.2946(5)(a). Seven other States have enacted similar provisions.[7]

B. Respondents' Claims And The Proceedings Below

Respondents are 27 individual plaintiffs whose complaints assert product liability claims under Michigan law against petitioners based on allegations

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[7] Tex. Civ. Prac. & Rem. Code Ann. § 82.007(b)(1) (creating a product liability defense for prescription drug companies unless the fact-finder determines the company "withheld from or misrepresented to [FDA] required information that was material and relevant to the performance of the product."); Ariz. Rev. Stat. § 12-701(B) (barring punitive damages against prescription drug company unless "the plaintiff proves, by clear and convincing evidence, that the defendant, either before or after making the drug available for public use, knowingly, in violation of applicable [FDA] regulations, withheld from or misrepresented to the administration information known to be material and relevant to the harm which the plaintiff allegedly suffered"); N.J. Stat. Ann. § 2A:58C-5(c) (same); N.D. Cent. Code § 32-03.2-11(6), (7)(a) (same); Ohio Rev. Code Ann. § 2307.80(C)(2) (same); Or. Rev. Stat. § 30.927(2) (same); Utah Code Ann. § 78-18-2(2) (same).

that they suffered personal injury from taking Rezulin (troglitazone), an FDA-approved prescription drug. See Pet. App. 332a-357a; JA 26-46.

1. Rezulin was indicated for the treatment of type 2 diabetes mellitus. Pet. App. at 336a, 343a, 353a, JA 32. "Type 2 diabetes is a life-threatening disease that affects 18 million Americans. It is a leading cause of coronary heart disease, blindness, kidney failure, and limb amputation." JA 27. FDA exercised regulatory oversight over Rezulin before and after approving it for marketing in the United States in 1997. See generally CDER, FDA, *Meeting No. 74 of Endocrinologic & Metabolic Drugs Advisory Committee* ("EMDAC") 38-49 (May 19, 2000), *available at* http://www.fda.gov/ohrms/dockets/ac/00/transcripts/3615t1.pdf (discussing regulatory history) (excerpted in Exh. B to Pl. Fisher's Opp. to Mot. for Judgment on the Pleadings).

The NDA for Rezulin was submitted to FDA in July 1996. JA 27-28. "[B]ecause [Rezulin] was the first in a new class of products to treat what is widely recognized as a serious and life-threatening disease"—type 2 diabetes mellitus—FDA accorded it "priority review," EMDAC Tr. 43-44, a status "given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists," FDA, *Fast Track, Accelerated Approval and Priority Review* (May 2006), *available at* http://www.fda.gov/oashi/fast.html.[8]

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[8] Priority review makes "therapeutically important drugs available at an earlier time," but "do[es] not compromise the standards for the safety and effectiveness of the drugs" subject to this review because "additional FDA attention and resources" are employed. FDA, *Fast Track*, *supra*.

During review of the NDA, and before approving Rezulin for marketing in the United States, FDA recognized that liver and cardiovascular risks were associated with the drug. JA 29-30; Press Release, U.S. Dep't of Health & Human Servs. ("HHS"), Rezulin To Be Withdrawn from the Market (Mar. 21, 2000) (FDA stating that "[s]evere liver toxicity has been known to occur with Rezulin since 1997"). Nonetheless, following its review of the overall risk-benefit profile, EMDAC recommended approval of Rezulin. JA 31; EMDAC Tr. 43. In January 1997, FDA agreed and approved Rezulin for concomitant use with insulin or other anti-diabetic drugs; in August 1997, FDA broadened Rezulin's approval to include "stand alone" use. JA 31-32; EMDAC Tr. 43.

Thereafter, FDA continued to review reports of adverse liver-related effects in Rezulin patients. Between November 1997 and June 1999, Warner-Lambert agreed to a series of labeling changes regarding these issues. Pet. App. 6a-7a; EMDAC Tr. 44-45; accord HHS, *supra* ("[i]n consultation with FDA," Rezulin's manufacturer "strengthened the drug's labeling several times and has recommended close monitoring of liver function in patients taking Rezulin"). Following another EMDAC review of all of the science in March 1999, FDA concluded that concomitant use of Rezulin and insulin had benefits that outweighed risks, but monotherapy no longer had a "positive benefit to risk perspective." EMDAC Tr. 45-46; HHS, *supra*.

In March 2000, Warner-Lambert voluntarily withdrew Rezulin from the United States market. This action followed the introduction of two new drugs for the treatment of type 2 diabetes. FDA concluded that Rezulin had become "outmoded" and therefore "no longer [had] a positive benefit to risk

calculus, in the face of newer drugs [that] appear to have a better safety profile." EMDAC Tr. 82-83; HHS, *supra*.

At no time did FDA determine that petitioners had improperly withheld material information from the agency. Nor did FDA opine that any non-disclosure affected the agency's decisions about whether Rezulin should continue to be marketed.

2. After Rezulin was withdrawn from the market, respondents, all Michigan residents, filed product liability actions against petitioners. Those complaints were all filed in or removed to the United States District Court for the Eastern District of Michigan, which had diversity jurisdiction over the actions. Respondents each allege that they suffered personal injury from their use of Rezulin and that petitioners are liable under various product liability theories as a result. See Pet. App. 6a; *id.* at 332a-357a; JA 35-45. Most pertinent here, the complaints also allege that petitioners "knowingly concealed material facts about the safety and efficacy of Rezulin from the FDA, which would have prevented its approval and/or resulted in its earlier removal from the market." Pet. App. 337a, 344a, 354a; see JA 33, 36, 43. There is no allegation that FDA *itself* ever determined that (i) petitioners violated federal law; (ii) petitioners improperly withheld information from FDA; or (iii) any purportedly withheld information would have affected, or later did affect, FDA's decisions about whether Rezulin could be marketed.

Following transfer of these cases by the Judicial Panel on Multidistrict Litigation to *In re: Rezulin Products Liability Litigation* (MDL No. 1348), before Judge Lewis Kaplan in the United States District Court for the Southern District of New York, petitioners moved for judgment on the pleadings.

Pet. App. 7a; see Fed. R. Civ. P. 12(c). In their motion, petitioners contended that Mich. Comp. Laws § 600.2946(5) provides a complete defense to respondents' claims. Petitioners further urged that respondents could not overcome petitioners' defense from product liability by availing themselves of Michigan's statutory exception for instances where a company "[i]ntentionally withholds from or misrepresents to [FDA] information concerning the drug that is required to be submitted under" the FDCA, and "the drug would not have been approved, or [FDA] would have withdrawn approval for the drug if the information were accurately submitted." Mich. Comp. Laws § 600.2946(5)(a). Invoking *Garcia* v. *Wyeth-Ayerst Laboratories*, 385 F.3d 961 (6th Cir. 2004), in which the Sixth Circuit held this exception to be preempted, petitioners argued that this provision is preempted under *Buckman Co.* v. *Plaintiffs' Legal Committee*, 531 U.S. 341 (2001).

In their response, respondents did not dispute that, absent the exception of Mich. Comp. Laws § 600.2946(5)(a), the Michigan provision otherwise would provide a complete defense to petitioners from respondents' state-law claims. Respondents did not contend that FDA itself had found petitioners to have intentionally misrepresented or withheld material information required by the FDCA. Nor did they claim that the agency concluded that it would have denied or withdrawn Rezulin's approval if any allegedly withheld information had been disclosed. Rather, respondents contended simply that Mich. Comp. Laws § 600.2946(5)(a) was not preempted under *Buckman* and that *Garcia* had been wrongly decided.

3. Following *Buckman* and *Garcia*, the district court held that petitioners were entitled to judgment

on the pleadings. It concluded that the Michigan exception is preempted where, as here, the agency itself has made no finding of fraud. Pet. App. 32a-36a. Absent preemption, the district court reasoned, plaintiffs would be unfettered to "litigate claims of fraud on the FDA in individual personal injury suits," directly contrary to the decision in *Buckman*. *Id.* at 35a. The district court noted that this would lead to numerous harmful effects, including the potential for "FDA's personnel to be drawn into those controversies on a case-by-case basis over and over again," and for FDA to "become the Food, Drug & Litigation Administration. The interference with the proper discharge of the mission that Congress created the FDA to perform would be enormous." *Id.* at 36a.

On appeal, the Second Circuit vacated the judgment entered by the district court. Pet. App. 1a-28a. Expressly parting with the analysis of the Sixth Circuit in *Garcia*, the Second Circuit held that the Michigan provision was not preempted because the Michigan plaintiffs were "not pressing 'fraud-on-the-FDA' claims" as in *Buckman*. *Id.* at 19a. Rather, it said that the plaintiffs were "asserting claims that sound in traditional state tort law." *Id.* The court acknowledged that the Michigan provision would require the trier-of-fact to find both that the manufacturer intentionally misrepresented material facts to FDA, and that FDA consequently would have denied or withdrawn approval of the drug had it been apprised of those facts. See *id.* at 19a-24a. The court further recognized that its approach would create "substantial inducements on the pharmaceutical industry to provide the federal agency with just the kind of information that troubled the *Buckman* and *Garcia* courts." *Id.* at 25a. Nevertheless, the court concluded that *Buckman* is not applicable and held

that respondents' showing under § 600.2946(5)(a) is not preempted.

On May 10, 2007, petitioners timely filed a petition for a writ of certiorari, which was granted on September 25, 2007. JA 47-48.

SUMMARY OF ARGUMENT

The Second Circuit's decision cannot be reconciled with this Court's decision in *Buckman Co.* v. *Plaintiffs' Legal Committee*, 531 U.S. 341 (2001). In *Buckman*, this Court held that state-law claims based on an allegation that the company made fraudulent misrepresentations to FDA were preempted. *Id.* at 344-45. This Court further held that "[s]tate-law fraud-on-the-FDA claims inevitably conflict with the FDA's responsibility to police fraud consistently with the Administration's judgment and objectives." *Id.* at 350. Permitting a trier-of-fact to determine whether a company violated federally imposed duties to the agency—a relationship "inherently federal in character"—cannot be squared with the role Congress delegated to FDA alone. *Id.* at 347-48.

Furthermore, this Court held that there is no presumption against preemption given the quintessentially federal character of the relationship between the federal agency and a company navigating FDA's approval regime. *Id.* (holding that no federalism concern was implicated, and no presumption against preemption applies, where the regulated entity's "dealings with the FDA were prompted by [federal law], and the very subject matter of [the regulated entity's] statements were dictated by that [federal] statute's provisions"). This Court further observed that permitting state law to inject itself into this federal relationship would lead to several undesirable practical consequences.

First, it would disrupt the delicate balance of statutory objectives FDA must strike in exercising its own review of whether there has been fraud and, if so, what degree of reaction is warranted. *Id.* at 348-50. Such "flexibility is a critical component" of FDA's work given that the FDCA charges FDA with "pursu[ing] difficult (and often competing) objectives." *Id.* at 349; *id.* at 350 (recognizing the need for the agency to "police fraud consistently with the Administration's judgment and objectives"). Second, permitting such claims would "dramatically increase" the burdens on manufacturers seeking to comply with FDA's approval regime "in the shadow" of the inevitably differing standards of various state tort regimes and jury determinations, thereby skewing regulatory incentives. *Id.* at 350-51.

Third, the threat of state-law determinations would encourage companies "to submit a deluge of information that [FDA] neither wants nor needs," particularly in light of the significant volume of information FDA already is charged with reviewing. *Id.* at 351. This would burden FDA and distract it from its core mission of regulating potentially life-saving and beneficial medical treatments according to the detailed existing standards Congress has charged it with implementing. Given the practical public health considerations the agency must weigh, more information is not always better. See generally 71 Fed. Reg. at 3935 (explaining that "theoretical hazards not well-grounded in scientific evidence can cause meaningful risk information to 'lose its significance'" and "[o]verwarning, just like under-warning, can . . . have a negative effect on patient safety and public health").

The Michigan provision cannot be reconciled with *Buckman* because it requires a fact-finder to

determine the very same inherently federal issues the *Buckman* Court held to be off-limits. Under the Michigan provision, for plaintiffs' claims to survive, plaintiffs must prove—and the trier-of-fact must find—three facts that would impinge upon the agency's role: (i) that the company "[i]ntentionally withholds from or misrepresents to [FDA]"; (ii) "information concerning the drug that is required to be submitted" under the various FDCA provisions FDA administers; and (iii) that FDA either "would not have . . . approved" or "would have withdrawn approval for the drug if the information were accurately submitted." Mich. Comp. Laws § 600.2946(5)(a). These inquiries intrude on the very same federal findings *Buckman* held to be solely within the agency's purview.

A State can choose to defer expressly to a federal regulatory scheme by shielding defendants from product liability claims when a matter is regulated by the Federal Government. What a State cannot do, however, is condition that defense on determinations by a fact-finder that intrude into an area of exclusive federal concern, *i.e.*, whether there has been "fraud-on-the-FDA." Because the Michigan provision trespasses on this area of exclusive federal concern, it is preempted.

ARGUMENT

I. FEDERAL LAW IMPLIEDLY PREEMPTS STATE LAW THAT REQUIRES THE FACT-FINDER TO DETERMINE WHETHER THE MANUFACTURER WITHHELD MATERIAL INFORMATION FROM THE AGENCY.

The Supremacy Clause of the United States Constitution provides that the laws of the United States "shall be the supreme Law of the Land[,] . . .

any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. Const. art. VI, cl. 2. Since *McCulloch* v. *Maryland*, 17 U.S. (4 Wheat.) 316, 427 (1819), "it has been settled that state law that conflicts with federal law is 'without effect,'" *Cipollone* v. *Liggett Group, Inc.*, 505 U.S. 504, 516 (1992) (quoting *Maryland* v. *Louisiana*, 451 U.S. 725, 746 (1981)). These preemption principles apply equally whether the federal provision is a statute or a regulation; in either case, if the state law hinders or frustrates federal objectives, the state law is preempted. See, *e.g.*, *Geier* v. *American Honda Motor Co.*, 529 U.S. 861, 885 (2000); *Hillsborough County* v. *Automated Med. Labs. Inc.*, 471 U.S. 707, 713 (1985).

Federal law impliedly preempts state law when the state law either actually conflicts with a federal statute or regulation, frustrates accomplishment of the provision's objectives, or touches upon a field in which the Federal Government has asserted exclusive regulatory authority. *Cipollone*, 505 U.S. at 516. The categories of implied preemption are not "rigidly distinct," and "field pre-emption may be understood as a species of conflict pre-emption." *English* v. *General Elec. Co.*, 496 U.S. 72, 79 n.5 (1990).[9] Whether analyzed in terms of invading a narrow field of exclusive federal concern or in terms of posing an impermissible and inevitable conflict

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[9] *See, e.g.*, *Gade* v. *National Solid Wastes Mgmt. Ass'n*, 505 U.S. 88, 104 n.2 (1992) (O'Connor, J., plurality opinion of four Justices) ("Although we have chosen to use the term 'conflict' pre-emption, we could as easily have stated that the promulgation of a federal safety and health standard 'pre-empts the field' for any . . . state law regulating the same safety and health issue."); *id.* at 115-16 (Souter, J., dissenting) (recognizing that conflict preemption may "present[] a situation similar in practical effect to that of federal occupation of a field") (internal quotation omitted).

with and obstacle to FDA's role in policing fraud in the regulatory regime it oversees, under the logic of *Buckman Co.* v. *Plaintiffs' Legal Committee*, 531 U.S. 341 (2001), the Michigan fraud-on-the-FDA provision is impliedly preempted by federal law.

The Michigan provision impermissibly requires the trier-of-fact to place itself in the shoes of the expert agency, and to speculate as to whether FDA would have found the manufacturer violated a federal duty arising from the FDCA by intentionally withholding from or misrepresenting to the agency material facts about the safety and efficacy of the drug. The fact-finder then must speculate as to whether this alleged "fraud on the agency" also would have *caused* FDA to deny initial approval or withdraw existing approval of the drug, as opposed to taking a more limited enforcement response. These determinations are indistinguishable from those held to be impermissible in *Buckman*. They intrude upon an area of exclusive federal concern and would interpose state law as an impermissible obstacle to FDA's congressionally delegated obligation to make precisely these expert findings.

A. The Federal Government Has Exclusive Authority To Regulate Compliance With FDA Disclosure Requirements.

The field involving a company's obligation to provide appropriate information to the federal agency regulating it is one in which there is a longstanding and overriding federal presence, not one the States have traditionally occupied. In this uniquely and exclusively federal space, if the federal agency is to perform its congressional mission, the agency must be free to decide how best to obtain needed information as well as how to punish those it determines fail to comply.

1. Recognizing that FDA bears the "responsibility to police fraud consistently with [its] judgment and objectives," *Buckman* held that an attempt by a third-party to show that FDA had been defrauded would "*inevitably conflict*" with this federal domain. 531 U.S. at 350 (emphasis added); see *id.* at 348 (observing that a "delicate balance of statutory objectives" is implicated in FDA enforcement decisions). As *Buckman* explained, the regulatory regime governing medical product approval was established by federal legislation, and the duty of the manufacturer to the agency is strictly federal in character. Thus, it is only appropriate that the regime should be administered solely by federal officials, in accordance with federal standards. See *id.* at 347 ("the relationship between a federal agency and the entity it regulates is inherently federal in character because the relationship originates from, is governed by, and terminates according to federal law"). Put another way, because the FDCA "touch[es] a field in which the federal interest is so dominant"—*i.e.*, policing fraud against the federal agency—involving duties created by federal law and owed to a federal agency, "the federal system will be assumed to preclude enforcement of state laws on the same subject." *Rice* v. *Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947). Federal law therefore preempts state law addressing the investigation and enforcement of a manufacturer's compliance with disclosure obligations during the FDA approval process. See *id.*; see also *Buckman*, 531 U.S. at 348-51; *Boyle* v. *United Techs. Corp.*, 487 U.S. 500, 505-06 (1988) (state law preempted where it sought to oversee duties owed to the Federal Government).

There is no role for States or private individuals to regulate a company's compliance with federal

disclosure requirements. Such matters are reserved to the federal agency. As detailed above, the FDCA empowers the agency alone to evaluate the sufficiency of submissions under the complex FDA regulatory scheme, to investigate suspected violations of disclosure requirements, 21 U.S.C. § 372, and to enforce those requirements as it sees fit. Central here, the FDCA vests enforcement power exclusively in the Federal Government: "[A]ll such proceedings for the enforcement, or to restrain violations, of this chapter shall be by and in the name of the United States." *Id.* § 337(a). Congress granted FDA a "variety of enforcement options to make a measured response"—ranging from administrative and civil penalties to seeking injunctive relief and criminal penalties. *Buckman*, 531 U.S. at 349; see 21 U.S.C. §§ 333, 336, 337.

Just as importantly, Congress has granted FDA discretion *not* to pursue formal enforcement measures after finding an FDCA violation. See 21 U.S.C. § 336; see also *Heckler*, 470 U.S. at 835 (FDA has "complete discretion . . . to decide how and when" to enforce the FDCA).[10] "This flexibility is a critical component of the statutory and regulatory framework under which the FDA pursues difficult (and often competing) objectives." *Buckman*, 531 U.S. at 349.

Respondents' effort to prove fraud-on-the-FDA under the Michigan provision intrudes upon this

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[10] Although private citizens may report suspected regulatory violations to FDA and petition it to take action, 21 C.F.R. § 10.30—and although Congress did grant state officials limited rights to bring suit to enforce certain prohibitions on misbranded *food*, 21 U.S.C. § 337(b)—nowhere does the federal statutory or regulatory scheme contemplate that private or state actors may enforce a drug manufacturer's compliance with federal disclosure obligations. *See Buckman*, 531 U.S. at 349.

field. It is thus preempted. In making their showing, respondents must prove that the manufacturer "[i]ntentionally withholds from or misrepresents to [FDA] information concerning the drug that is required to be submitted under the [FDCA]" and that "the drug would not have been approved, or [FDA] would have withdrawn approval for the drug if the information [had been] accurately submitted." Mich. Comp. Laws § 600.2946(5)(a).

Thus, necessary to a determination that this exception applies are findings that (1) federal law required the manufacturer to disclose certain information to the agency, (2) the manufacturer failed to produce that information to the agency, and (3) the failure to disclose was material to the agency's approval of the drug. See *id.*; *Garcia*, 385 F.3d at 964-66. Each one of these findings involves the state fact-finder in the interpretation and application of federal statutes and regulations that are, by congressional directive, subject exclusively to federal oversight. See Mich. Comp. Laws § 600.2946(5)(a) (citing, *inter alia*, 21 U.S.C. §§ 355-360); cf. 21 U.S.C. § 337(a).

Unlike the state laws at issue in cases in which this Court has declined to find preemption, the Michigan provision at issue here does not regulate public health and safety. Rather, it trespasses directly on an area of exclusive federal concern. See Mich. Comp. Laws § 600.2946(5)(a); cf., *e.g.*, *Silkwood* v. *Kerr-McGee Corp.*, 464 U.S. 238, 256 (1984) (state law allowed persons injured by nuclear incidents to recover from operators).[11] The only effect of this

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[11] As *Buckman* explained, *Silkwood* is readily distinguishable. First, nowhere did the state law at issue in *Silkwood* require the plaintiff to demonstrate that *federal* duties had been violated to

provision is to police and enforce compliance with FDA disclosure rules. See *Garcia*, 385 F.3d at 966. But this is not a valid role for state legislation: investigating and enforcing compliance with FDA regulations concerning disclosures to FDA is (and always has been) a matter of exclusive federal concern. *Buckman*, 531 U.S. at 347-53; *Kobar ex rel. Kobar* v. *Novartis Corp.*, 378 F. Supp. 2d 1166, 1173 (D. Ariz. 2005) (both the common law fraud-on-the-FDA claim at issue in *Buckman*, and a state statute that requires plaintiffs to prove fraud-on-the-FDA to avoid a bar on punitive damages, "place state courts, as finders of fact, in the uncomfortable and difficult position of having to answer the question of what role, if any, the allegedly withheld information would have played in the FDA's complicated approval process").

2. The problems that would flow from a contrary conclusion, under which state juries would be allowed to judge a manufacturer's compliance with disclosure obligations to FDA, are manifest. Interpretation of agency rules concerning such disclosures, which often hinge on application of specialized scientific and public health knowledge, would be entrusted not to the expert agency alone but to independent lay fact-finders in the different States. *Buckman*, 531 U.S. at 350-51. A manufacturer could no longer be certain

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proceed with her claims. *See Buckman*, 531 U.S. at 352 (inquiry in *Silkwood* "was not based on any sort of fraud-on-the-agency theory"). Here, in contrast, the fact-finder is required to find a violation of a federal duty owed to the agency alone and then to further determine how the agency would have reacted to the violation. *See* Mich. Comp. Laws § 600.2946(5)(a). Second, the federal regime at issue in *Silkwood* contained no provision comparable to Section 337(a), which provides "clear evidence" that the FDCA is to be "enforced exclusively by the Federal Government." *Buckman*, 531 U.S. at 352.

that adherence to the agency's interpretations concerning its own regulations about disclosures to that agency would guarantee a finding of compliance with those regulations. *Id.* To defend against a determination of non-compliance by a lay fact-finder—better ensuring its prospects of prevailing in eventual litigation through motions practice or at trial—the manufacturer would have a substantial incentive to submit as much information as possible to the agency. See *id.* at 351.[12] When a fact-finder is permitted to determine what *should have* been submitted to an agency and what the agency *might have* found material--as the Michigan provision requires—the party interacting with the agency would "have an incentive to submit a deluge of information that the Administration neither wants nor needs, resulting in additional burdens on the FDA[]." *Id.*

Moreover, instead of agency officials having final word on a manufacturer's compliance with FDCA-imposed duties concerning disclosures to FDA—and whether, even in the face of noncompliance, the scientific data nonetheless support keeping the drug on the market—lay jurors nationwide would be permitted to make shadow determinations on these sensitive issues. The force of the agency's expertise, in turn, would be diminished and Congress's interest

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[12] The Second Circuit acknowledged as much. *See* Pet. App. 25a ("So long as a court or jury is *allowed to consider* evidence of fraud against the FDA . . there will be substantial inducements on the pharmaceutical industry to provide the federal agency with just the kind of information that troubled the *Buckman* and *Garcia* Courts."). Nevertheless, it opined that "the incentive to flood the FDA appreciably escalate[s]" "[o]nly when proof of fraud is by itself *sufficient* to impose liability." *Id.* To the contrary, the incentive will exist whenever a fact-finder is required to make the same determination FDA must make.

in uniform drug regulation would be undermined, if States could impose liability whenever they deem that a drug's withdrawal would have been appropriate because of perceived fraud-on-the-agency.

This problem is particularly acute in the context presented here, in which the agency already is charged with analyzing detailed information it considers important and rendering sensitive public health judgments. In this highly regulated context, more is not necessarily better. Instead, additional state-law requirements for the disclosure of information to the federal agency can erode and disrupt the careful assessment the expert agency already is required to make.

Moreover, to retain any semblance of a uniform national scheme of drug regulation, FDA would be forced to monitor, assess, and possibly engage in a multitude of lawsuits across the country. FDA consistently might feel (or be) compelled to make its officials available to testify in litigation proceedings to refute improper speculation about whether (i) data had been misrepresented or withheld by a manufacturer, (ii) the manufacturer even had a federal duty to disclose such data, and (iii) the agency would have declined or withdrawn approval of the drug even if a federal duty had been violated. FDA would become, in the words of the district court, the "Food, Drug & Litigation Administration" with litigation burdens creating "enormous" interference with the agency's functions. Pet. App. 35a-36a.

It is inconceivable that Congress intended these results. To the contrary, the statutory scheme demonstrates conclusively that Congress anticipated that only federal officials would have authority to investigate and enforce federal regulations concerning required disclosures to the FDA. 21

U.S.C. §§ 337(a), 336; cf. *Cipollone*, 505 U.S. at 516 ("[t]he purpose of Congress is the ultimate touchstone" in a preemption analysis) (internal quotation omitted). Because the Michigan fraud-on-the-FDA provision requires a fact-finder to decide whether a manufacturer complied with disclosure requirements to FDA, and whether that mattered to FDA's approval, it intrudes on a field committed exclusively to federal control. It is, therefore, preempted. See *Buckman*, 531 U.S. at 350-51.

B. The FDCA Regime Designed By Congress Would Be Unconstitutionally Obstructed If Fact-Finders Were Allowed To Make The Determinations Required By Michigan's Exception To Its Statutory Bar To Product Liability.

The fraud-on-the-FDA determination required by the Michigan provision also conflicts with, and poses an impermissible obstacle to, FDA's uniform enforcement of the FDCA. This Court has recognized that "even if Congress has not occupied the field, state law is naturally preempted to the extent of any conflict with a federal statute." *Crosby* v. *National Foreign Trade Council*, 530 U.S. 363, 372 (2000). Implied conflict preemption exists both where it would be impossible for a party to comply with both state and federal law, and "where 'under the circumstances of a particular case, the challenged state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.'" *Id.* at 372-73 (alterations omitted) (quoting *Hines* v. *Davidowitz*, 312 U.S. 52, 67 (1941)).

As shown above, through the FDCA, Congress has delegated to FDA the power to determine whether prescription drugs are sufficiently safe and effective

to be marketed in the United States, and to remain on the market. *Supra* at 3-11; see also *Brown & Williamson Tobacco Corp.*, 529 U.S. at 165 (Breyer, J., dissenting) (endorsing view that FDCA "'is a purposefully broad delegation of discretionary powers by Congress'"). Central determinations within FDA's purview are whether a manufacturer has satisfied pre- and post-market disclosure requirements. See, *e.g.*, 21 U.S.C. § 355(e), (k); 21 C.F.R. § 314.50.

FDA never found that petitioners failed to comply with pre- or postmarketing disclosure requirements regarding Rezulin. Moreover, FDA never withdrew approval for the marketing of Rezulin in the United States based on any failure of disclosure by petitioners. Yet respondents cannot recover under the Michigan statute unless they could prove, and the trier-of-fact were to find, exactly the opposite. See Mich. Comp. Laws § 600.2946(5)(a). To allow the trier-of-fact to make these determinations would intrude on, and interfere with, FDA's core functions as delegated by Congress. Because the Michigan statutory exception requires the trier-of-fact to reach determinations "intimately blended and intertwined with the responsibilities of the national government," state law "'must yield'" to the expert federal agency acting on the same subject under the congressional design. *Hines*, 312 U.S. at 66 (quoting *Gibbons* v. *Ogden*, 22 U.S. (9 Wheat.) 1, 211 (1824)).

1. In *Buckman*, this Court held that attempts to prove FDA was defrauded "conflict with, and are therefore impliedly pre-empted by, federal law." 531 U.S. at 348. There, the plaintiffs attempted to show that they had been injured by the fraudulent conduct of a consultant the manufacturer had retained to assist it in obtaining FDA approval to market a medical product. The plaintiffs argued that had the

consultant not defrauded FDA during the approval process, the product causing their injury never would have come to market. As discussed, the *Buckman* Court concluded that policing fraud on federal agencies is a function reserved to the Federal Government, and was delegated to FDA in the FDCA context. See *id.* at 347-48. Recognizing that the agency itself bears the "responsibility to police fraud consistently with [its] judgment and objectives," the opinion made clear that any attempted showing by a third-party that FDA had been defrauded would upset the "delicate balance of statutory objectives" implicated in FDA decisionmaking under the FDCA. *Id.* at 348, 350.

Indeed, the likelihood of conflict preemption is increased whenever a plaintiff seeks to have lay fact-finders reformulate through state law the technical balances reached by federal agencies. See, *e.g.*, *Geier*, 529 U.S. at 877-82 (holding obstacle preemption applies where Department of Transportation applied its expertise and considered delicate balance of regulatory issues); *Capital Cities Cable, Inc.* v. *Crisp*, 467 U.S. 691, 714 (1984) (holding preemption applies where Federal Communications Commission "attempted to strike a balance" among regulatory concerns in serving an "important and substantial federal interest"); *Ray* v. *Atlantic Richfield Co.*, 435 U.S. 151, 177 (1978) (holding preemption applies where congressional scheme evidenced desire to have regulation set by the Secretary of Transportation who had "an overview of all the possible ramifications" and "act[ed] only after balancing all of the competing interests"); cf. *Leslie Miller, Inc.* v. *Arkansas*, 352 U.S. 187, 190 (1956) (per curiam) (state's exercise of "virtual power of review" over federal determinations would frustrate congressional intent).

A contrary approach would lead to numerous undesirable practical consequences detailed above. First, it would disrupt FDA in determining whether a violation has occurred and, if so, the proper level of response (if any). *Buckman*, 531 U.S. at 348-50. Second, it would "dramatically increase" the burdens on manufacturers endeavoring to comply with federal standards in the shadow of competing and inconsistent state-law demands as to that very same federal system. *Id.* at 350-51. Third, pressures from these shadow regimes would encourage companies "to submit a deluge of information that [FDA] neither wants nor needs." *Id.* at 351. Additionally, FDA would be distracted from its congressional mission by inevitable efforts by courts and private parties to supplant federal regulatory processes by having FDA address allegations of fraud in the context of ongoing private litigation. These overlapping and inconsistent state-law pressures distort the expert agency making these determinations on its own terms according to its own regulatory priorities, as is the intention of the federal drug regime.

2. These principles apply forcefully, and dispositively, here. For a plaintiff to satisfy Michigan's statutory exception, his or her claims require the fact-finder to make precisely the determinations found preempted in *Buckman*. Before the plaintiff is allowed to prove his or her case—by establishing a tort claim—he or she bears the burden of convincing a fact-finder that FDA was materially defrauded by the defendant. See Mich. Comp. Laws § 600.2946(5)(a). This showing is not remotely akin to proving a "traditional" state-law fraud claim involving private parties to a dispute. Whether the allegedly withheld materials should have been disclosed to FDA is not determined vis-à-vis the

relationship between plaintiff and defendant. Rather, just as in *Buckman*, plaintiffs must show that the manufacturer or other regulated entity violated a *federal duty* by withholding or misrepresenting the information in question (*i.e.*, information "required to be submitted under the federal food, drug, and cosmetic act") to the federal agency. Cf. *Boyle*, 487 U.S. at 505-06 (holding that state law was preempted where it sought to oversee duties owed to the Federal Government).

Moreover, the Michigan statute requires the same speculation about proximate cause that was held to be impermissible in *Buckman*. That is, the fact-finder must determine that, had the information not been misrepresented or withheld, then *FDA* would have taken one of two specific actions: (i) denied approval, or (ii) withdrawn approval. But permitting a fact-finder to speculate whether disclosure of the misrepresented information would have led to denial or withdrawal of the NDA is a frontal attack on FDA's authority that cannot be reconciled with Congress's charge. The fact-finder essentially would be required to determine either that FDA (i) never should have approved the drug, or (ii) should have removed it from the market earlier, because of allegedly fraudulent disclosures to the agency. But, it is axiomatic that "one of the [FDCA]'s core objectives" was to delegate these determinations exclusively to FDA. *Brown & Williamson Tobacco Corp.*, 529 U.S. at 133; see 21 U.S.C. § 337(a); *Hynson, Westcott & Dunning*, 412 U.S. at 627 (Congress created FDA as the "expert agency" to regulate drugs).

Lay jurors necessarily lack the scientific expertise and perspective FDA draws upon. They simply cannot reliably assess whether FDA would have

disapproved an NDA or withdrawn a drug's approval because of alleged fraud-on-the-agency. Cf. *Heckler*, 470 U.S. at 831 (agency's decision not to enforce generally is "unsuitabl[e]" for judicial review because it "often involves a complicated balancing of a number of factors which are peculiarly within [the agency's] expertise"). Yet if the fact-finder were to reach these conclusions, the defendant would be exposed to inappropriate and potentially massive liability. Such liability could even have the potential to drive a product off the market, although FDA would not want that result.

Furthermore, there are reasons to believe that lay persons would speculate inaccurately that FDA would select its most severe enforcement measures from the panoply of options available in its arsenal to combat fraud, even though the agency might not do so. See *Buckman*, 531 U.S. at 349-50; 21 U.S.C. § 336 (granting agency discretion to bypass formal enforcement actions "whenever [it] believes that the public interest will be adequately served by a suitable written notice or warning"); see also, *e.g.*, *A.L. Pharma, Inc.* v. *Shalala*, 62 F.3d 1484 (D.C. Cir. 1995) (upholding FDA's discretionary decision not to withdraw drug approval as penalty for misrepresentation). Specifically, a jury that already has determined that a defendant "intentionally misrepresented or withheld" required information may be predisposed to overestimate the gravity of the information in question. That is, the jury's reaction to the perceived misconduct may cause it to conclude—wrongly—that FDA's enforcement would have been drastic because the fact-finder necessarily lacks perspective beyond the individual patient alleged to have been injured in the case before them. See generally *Carroll* v. *Otis Elevator Co.*, 896 F.2d

210, 215-16 (7th Cir. 1990) (Easterbrook, J., concurring) (recognizing the tendency of jurors in product liability cases to focus on "today's injury" rather than probabilities, thus rendering "invisible" the individuals who would have been harmed had the allegedly defective product not been on the market). FDA, by contrast, (i) is keenly aware of the scores of patients for whom the drug has been successful, thus allowing the agency to make an overall public health risk-benefit calculation that may be lost on the lay jury in a lone case, and (ii) when considering whether an NDA should be denied or withdrawn must weigh certain individual patients experiencing side effects against the overall public health risks and benefits of alternative therapies or having no potentially viable treatment available. In short, the jury's perspectives on the propriety of approval or withdrawal can be overwhelmingly shaped by a response to the exigencies in a single case. Pursuant to Congress's command, however, FDA must consider the overall public health.[13]

In sum, permitting a fact-finder to determine, through lay speculation, (i) whether certain data was "required to be submitted under" the FDCA regime

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[13] Absent these protections, it is relatively easy for plaintiffs' counsel to capitalize on perceived defects in a manufacturer's submissions to FDA to create jury hostility. Plaintiffs can seize on stray documents that were not submitted—even where FDA was fully apprised of an issue or would not have viewed the unsubmitted documents as material. Yet it is extremely difficult for a manufacturer to prove a negative, that is, that FDA was *not* defrauded. Making such a showing is particularly difficult given FDA's understandable reluctance to expose its officials to testifying in tort litigation. *See* 21 C.F.R. § 20.1; *Giza* v. *Secretary of Health, Educ. & Welfare*, 628 F.2d 748, 750-52 (1st Cir. 1980) (affirming refusal to compel testimony of FDA official in product liability action).

and (ii) whether FDA would have denied or withdrawn approval of the drug had the information been presented differently, are the very inquiries foreclosed by *Buckman* because they would present severe obstacles to the agency appropriately accomplishing its regulatory function.

3. Nothing in the concurring opinion in *Buckman* would lead to a different result here. That opinion suggested that the preemption principles discussed here may be diminished "if, prior to the instant litigation, [1] *the FDA had determined* that petitioner had committed fraud [on the agency] *and* [2] had then taken the necessary steps to remove the harm-causing product from the market." 531 U.S. at 354 (Stevens, J. and Thomas, J., concurring in the judgment) (emphasis added). Where "FDA determines both that fraud has occurred and that such fraud requires the removal of a product from the market," the concurrence posited, state claims would supplement, not encroach upon, the federal regulatory scheme. *Id.* Cf. *Medtronic, Inc.* v. *Lohr*, 518 U.S. 470, 492-502 (1996) (allowing, in the absence of express or field preemption, state-law tort claims to proceed where they paralleled federal law); *Garcia*, 385 F.3d at 966 ("[T]he same concerns" of inter-branch meddling that animated *Buckman* "do not arise when the *FDA itself* determines that a fraud has been committed on the agency during the regulatory-approval process.").

In this case, however, FDA did not find that petitioners have committed fraud-on-the-agency, let alone announce that it was withdrawing drug approval or that it never would have approved the NDA in the first instance on account of such fraud. Indeed, respondents have never claimed—either in their complaints, or in their opposition to petitioners'

motion for judgment on the pleadings, or in their responses to the Second Circuit, or their opposition to the petition for certiorari in this Court—that FDA itself found petitioners had committed fraud-on-the-agency. Because the rule endorsed by the concurring Justices in *Buckman* therefore has no bearing here and would provide no relief to respondents in the present case, this Court need not address such a potential exception to preemption. Accordingly, should this Court hold that Michigan's statutory exception is preempted as applied here, it need not remand this case for further proceedings. Rather, the Second Circuit should be reversed, and the judgment of the district court reinstated.

II. THE SECOND CIRCUIT'S ANALYSIS IS FLAWED AND IRRECONCILABLE WITH *BUCKMAN*.

Although the opinion of the court of appeals below points to a number of distinctions between the circumstances here and in *Buckman*, none makes a difference to the core point in both cases: lay juries are not entitled to adjudicate whether there has been a material fraud-on-the-federal agency.

The court of appeals gave three inter-related, and purportedly "crucial," distinctions for avoiding *Buckman* preemption here. See Pet. App. 18a. First, it framed its analysis with a "presumption against preemption" because it viewed this case as involving ordinary and traditional State health and safety considerations, rather than an inherently federal question. *Id.* at 18a-19a. Second, the Second Circuit considered it significant that respondents bring underlying "traditional" common law tort claims premised on petitioners owing a duty to them, whereas in *Buckman* the fraud-on-the-FDA claim rested on a duty from the company to the agency

alone. *Id.* at 19a-23a. Third, the court opined that there was a meaningful distinction between proof of fraud-on-the-agency as a cause of action (the setting in *Buckman*) versus proof of fraud-on-the-agency to rebut an affirmative defense (as it framed the issue here). *Id.* at 23a-24a. These distinctions, all versions of the same essential point, collapse under a single analytic flaw: they ignore the impermissible federal-law inquiry that is inevitably required by the Michigan provision.

A. There Is No Presumption Against Preemption In This Context.

This Court in *Buckman* already conclusively held that there is no presumption against preemption because "[p]olicing fraud against federal agencies is hardly 'a field which the States have traditionally occupied.'" *Buckman*, 531 U.S. at 347 (quoting *Rice*, 331 U.S. at 230); see § I, *supra*. Nonetheless, the Second Circuit opinion places an impermissible "thumb on the scale" by framing respondents' claims as simply invoking the traditional "province of the states to safeguard the health and safety of their citizens," rather than a federal issue. Pet. App. 2a; see *id.* at 3a (describing common law liability as "the bedrock of state regulation"); *id.* at 18a-19a. This is wrong for at least two reasons.[14]

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[14] Even if a presumption against preemption applied—and it does not—the uniquely federal circumstances at issue here still would overcome any such presumption and compel preemption. *See, e.g.*, *Ray*, 435 U.S. at 157, 160, 163-64 (holding that, notwithstanding the application of a presumption against preemption, state-law requirements for vessels were preempted by federal law given the federal character of the relationship at issue (between vessels and the Coast Guard)).

1. The Michigan provision at issue here does not "regulate health and safety." To the contrary, it purports to regulate, as a matter of state law, a strictly federal matter: a company's compliance with federal disclosure standards under the FDCA that FDA alone is empowered to enforce. *Buckman* held that there is no presumption against preemption where a lay jury is asked to determine whether there has been a material fraud against a federal agency. This follows because the manufacturer's relationship with the agency under the federal scheme is "inherently federal in character" and "[p]olicing fraud against federal agencies is hardly 'a field which the States have traditionally occupied.'" *Buckman*, 531 U.S. at 347 (quoting *Rice*, 331 U.S. at 230).

The Second Circuit, however, held that, because the Michigan provision "cannot reasonably be characterized as a [S]tate's attempt to police fraud against the FDA," but was passed as part of an effort to "'regulat[e] matters of health and safety,'" a presumption against preemption applied. Pet. App. 18a-19a. To the contrary, the very premise of the underlying Michigan provision shielding drug manufacturers from product liability claims is to defer expressly to the Federal Government's unique role in regulating highly specialized medical products. In any event, the court below cited no authority holding that a presumption against preemption is assessed by the supposed *purposes* rather than by the *operation and effect* of the state-law provision at issue. In fact, the actual function of the provision is what matters. Cf., *e.g.*, *American Ins. Ass'n* v. *Garamendi*, 539 U.S. 396, 418 (2003) (examining the *effect* of state law on the federal interest); *Egelhoff* v. *Egelhoff ex rel. Breiner*, 532 U.S. 141, 147 (2001) (same).

Even if the Second Circuit were correct to analyze the purposes of the Michigan fraud-on-the-FDA provision in the abstract rather than the practical effect of the exception at issue here, it impermissibly ignores that the exception requires that the fact-finder engage in the same analysis found impermissible in *Buckman*. In doing so, the trier is required to determine issues "inherently federal in character"—namely, whether the defendant's "dealings with the FDA [which] where prompted by the [FDCA], and the very subject matter of [defendant's] statements [which] were dictated by that statute's provisions" violated *federal law*. *Buckman*, 531 U.S. at 347-48.

2. Although the Court need not look beyond the clear holding of *Buckman* to determine that no presumption against preemption applies in this context, there is yet another reason why the Second Circuit's presumption is wrong. No presumption against preemption applies where, as here, the state law stands as an obstacle to a federal scheme.

This notion is particularly striking in the context present here, because state law is seeking to regulate an area in which there has been "a history of significant federal presence." *United States* v. *Locke*, 529 U.S. 89, 108, 111 (2000) (citing *Rice*, 331 U.S. at 230). For more than a century, the Federal Government has regulated drugs in the United States market. See generally *United States* v. *Walsh*, 331 U.S. 432, 434 (1947) ("[t]he [FDCA] rests upon the constitutional power resident in Congress to regulate interstate commerce" and Congress has regulated drugs "[t]o the end that the public health and safety might be advanced") (citing Article 1, § 8, cl. 3).

When a field has long been subject to federal control, "there is no beginning assumption that

concurrent regulation by the State is a valid exercise of its police powers." *Locke*, 529 U.S. at 108; see *Buckman*, 531 U.S. at 347. In such a circumstance, "one can assume that Congress or an agency ordinarily would not intend to permit a significant conflict" between federal and state law. *Geier*, 529 U.S. at 885; see *Felder* v. *Casey*, 487 U.S. 131, 138 (1988) ("Under the Supremacy Clause of the Federal Constitution, '[t]he relative importance to the State of its own law is not material when there is a conflict with a valid federal law,' for 'any state law, however clearly within a State's acknowledged power, which interferes with or is contrary to federal law, must yield.'") (citations omitted).[15]

B. There Is No Meaningful Difference Between The Inquiry At Issue Here And In *Buckman*.

The Second Circuit also distinguished *Buckman* on the basis that respondents "assert[] claims that sound in traditional state tort law" and thus involve duties owed by the manufacturer to respondents, see Pet. App. 19a-20a, whereas, in *Buckman*, the plaintiffs sought to recover based on violation of a duty owed to FDA alone, *id.* at 20a. The court below also posited that in a pure FDA-fraud case (*Buckman*), "proof of fraud against the FDA is *alone sufficient* to impose

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[15] Notwithstanding some general debate about whether a presumption against preemption applies in the implied preemption context, *see generally Crosby*, 530 U.S. at 374 n.8 (declining to resolve whether a presumption against preemption applied in the context of implied conflict preemption); *see also Engine Mfrs. Ass'n* v. *South Coast Air Quality Mgmt. Dist.*, 541 U.S. 246, 256 (2004) (recognizing "not all Members of this Court agree" about the role of the "'presumption against preemption'"), at a minimum, there is no role for such a presumption as to the quintessentially federal inquiry at issue in this case.

liability," but here respondents' "traditional" tort claims required them to make out "freestanding allegations of wrongdoing." *Id.* at 20a-21a. This wooden interpretation of *Buckman* improperly elevates form over function and disregards the effect of the pertinent federal law inquiry in both circumstances.

1. Contrary to the Second Circuit's view, it makes no difference to the analysis that the claims in this case find their "'vintage'" in traditional tort law. See Pet. App. 20a. That respondents ultimately must prove a violation of a manufacturer's traditional state-law duty to prevail on their claims does not obviate the fact that to be *permitted* to proceed under Michigan's product liability law respondents must prove a violation of "a newly-concocted duty between a manufacturer and a federal agency." *Id.*; see Mich. Comp. Laws § 600.2946(5)(a). Accordingly, as in *Buckman*, respondents' recovery irreducibly depends on proving to a state fact-finder that petitioners materially violated federal requirements. See 531 U.S. at 348-49; *id.* at 352-53; *Garcia*, 385 F.3d at 966 ("'state tort remedies *requiring* proof of fraud committed against the FDA are foreclosed since federal law preempts such claims'") (quoting district court).

As noted, the Michigan statute amended Michigan's earlier common law product liability regime by interposing a general defense to product liability for manufacturers, and creating a limited exception when the manufacturer is shown to have committed fraud-on-the-FDA during the drug approval process. Mich. Comp. Laws § 600.2946(5); *Taylor* v. *SmithKline Beecham Corp.*, 658 N.W.2d 127, 130-31 (Mich. 2003). By so doing, this amendment in effect created the necessary pathway to relief for plaintiffs,

requiring proof both that the product was defective *and* that the manufacturer had violated FDA disclosure rules. See *Garcia*, 385 F.3d at 965-66. The state-law tort causes of action asserted by respondents would not go forward but for respondents successfully proving a "fraud-on-the-FDA."

It does not matter to the analysis that the cause of action in *Buckman* was denominated fraud-on-the-FDA, while the cause of action in this case incorporates agency fraud as a prerequisite to traditional tort liability. Nothing in *Buckman* suggests that its holding should apply only when fraud-on-the-FDA is a "positive" element of a cause of action's required proof. Rather, the focus in *Buckman* was on the *practical effect* of the adjudication of the claim: whether it would involve the fact-finder in an area committed to federal regulation, thereby creating an inevitable conflict with the federal scheme. 531 U.S. at 348-51; see *id.* at 353 (federal inquiry was "a critical element of [plaintiff's] case"). The Second Circuit's fixation on what respondents here pleaded (violations of a state duty in addition to federal duty) imbues the procedural posture of *Buckman* with far more significance than is warranted in light of this Court's analysis in striking down the state-law claims. In any event, this distinction is moot because respondents actually plead fraud-on-the-FDA in their complaints. See Pet. App. 337a, 344a, 354a; JA 33, 36, 43.

Adopting the Second Circuit's formalistic approach would lead to absurd results. Under it, a State would be prohibited from amending a common law tort cause of action to incorporate fraud-on-the-FDA as a formal element of a claim (as the State did in *Buckman*). Inexplicably, however, a State would be

permitted to achieve the same result by amending the cause of action to incorporate fraud-on-the-FDA as a prerequisite to liability (as the State did here). See Pet. App. 19a-21a. This approach is squarely at odds with the functional approach of *Buckman*. It would, moreover, render preemption analysis nothing more than a semantic game, a system that state legislatures (and, to a large degree, plaintiffs) could gerrymander around simply by phrasing fraud-on-the-FDA as a condition precedent to liability, rather than a formal element of the claim. There is no basis to permit such an end-run around the analysis of *Buckman*.

The fundamental problem with the claims at issue in *Buckman* was not that the plaintiffs there failed to "rely[] on traditional state tort law which had predated the federal enactments" but that, "[o]n the contrary, the existence of these federal enactments [was] a critical element of their case." *Buckman*, 531 U.S. at 353. The same concern applies here. Respondents may bring traditional state tort causes of action, but those claims can proceed only if respondents can prove that the manufacturer failed to comply with federal statutory and regulatory requirements. Mich. Comp. Laws § 600.2946(5)(a); see Pet. App. 20a-21a. This is no different than *Buckman*. In both circumstances, the "federal enactments [are] a critical element," without which the plaintiffs' claims cannot go forward. *Buckman*, 531 U.S. at 353.

2. Second, the court below erred in purporting to distinguish *Buckman* on the basis that the cause of action at issue there was premised exclusively on fraud against FDA and had no non-federal elements. Pet. App. 20a. No such distinction exists. A showing of fraud-on-the-FDA was as necessary for plaintiffs to

prove their claims in *Buckman* as it is necessary for respondents to maintain their claims under Michigan law. In neither case, though, would proving such fraud alone be sufficient to trigger liability. Rather, the plaintiffs in *Buckman* also were required to prove, in addition to the violation of the federal duty itself, that the violation led to marketing a product that presented an unreasonable risk of injury, and that harm was caused to the plaintiffs as a result. See *In re Orthopedic Bone Screw Prods. Liab. Litig.*, 159 F.3d 817, 826-29 (3d Cir. 1998) (discussing elements of fraud-on-the-FDA claim), *rev'd on other grounds sub nom. Buckman*, 531 U.S. 341; see also *Buckman*, 531 U.S. at 347 (noting claims required proof that products were used "to the plaintiffs' detriment"). These elements of proof mirror those necessary to impose liability on a defendant under the Michigan product liability scheme, *i.e.*, that, as a result of federal law violations, defendant was able to market a product with an unreasonable risk of harm, and that plaintiff was harmed as a consequence. See Mich. Comp. Laws § 600.2946(5)(a); *Gregory* v. *Cincinnati Inc.*, 538 N.W.2d 325, 329 (Mich. 1995); *Reeves* v. *Cincinnati, Inc.*, 439 N.W.2d 326, 329 (Mich. Ct. App. 1989).

The only possible divergence between the claims here and those in *Buckman* is that the latter provided for damages based directly upon the fraud itself, see 531 U.S. at 343, 347, while the former treats fraud as a condition precedent to recovery, independent of the damages calculation, see Mich. Comp. Laws § 600.2946(5)(a). But such a distinction, assuming it exists, is without difference. As discussed, both causes of action require that the fact-finder pass upon the manufacturer's compliance with FDA disclosure requirements. That this element forms part of the

causal chain of liability in one claim (*Buckman*) but stands as a condition precedent to liability in the other (here) does not alter the fact that both causes of action contemplate—indeed, demand—that the fact-finder infringe on an area dedicated exclusively to federal regulation. See *Garcia*, 385 F.3d at 966; see also 21 U.S.C. § 337(a); *Buckman*, 531 U.S. at 349-51. *Buckman* is materially indistinguishable from, and therefore controls, this case. *Garcia*, 385 F.3d at 966.

3. Nothing in the Second Circuit's analysis alters why *Buckman* is controlling here. The claims in both cases share the same essential attribute: they demand proof of fraud-on-the-agency as a pre-requisite to a finding of liability. 531 U.S. at 349-53; see also *Garcia*, 385 F.3d at 965-66 (concluding that any distinctions between the Michigan regime and the cause of action at issue in *Buckman* were "immaterial in light of *Buckman*" because "'*Buckman* teaches that state tort remedies requiring proof of fraud committed against the FDA are foreclosed since federal law preempts such claims'") (quoting district court). Here, as in *Buckman*, the Michigan exception requires a lay jury to pass on the manufacturer's noncompliance with FDA disclosure requirements, encroaching upon a field of exclusive federal control, and inevitably conflicting with federal statutory and regulatory provisions. *Buckman*, 531 U.S. at 349-53. Rather than governing the relationship between pharmaceutical companies and Michigan citizens, the provision here and the claims in *Buckman* impermissibly seek to regulate the relationship between pharmaceutical companies *and the FDA*.

The federal-law inquiry put to the trier-of-fact under the Michigan exception impermissibly allows juror "speculation about what [a federal agency] might have done had it been faced with the facts of

this case." *Arkansas La. Gas Co.* v. *Hall*, 453 U.S. 571, 578-79 (1981). This is not an area in which "coordinate state and federal efforts exist within a complementary administrative framework, and in the pursuit of common purposes." *New York State Dep't of Soc. Servs.* v. *Dublino*, 413 U.S. 405, 421 (1973).[16] Thus, applying the rule in *Buckman* here would not, as the Second Circuit suggested, "gut[]" state tort law or otherwise modify the "traditional state law duties between pharmaceutical companies and their consumers." Pet. App. 20a. It simply limits state law from permitting fact-finders to invade the exclusively federal province at issue here.

C. *Buckman* Did Not Hinge On Fraud-On-The-Agency Being A Cause Of Action, Rather Than A Showing Required To Rebut An Affirmative Defense.

In a variation of the theme just discussed, the Second Circuit also deemed *Buckman* distinguishable because, under Michigan's provision, fraud-on-the-agency "is not even an *element* of a products liability claim." Pet. App. 23a. The court of appeals found it significant that the statute "does no more than create a defense that drug makers may invoke, if they so decide, and that it is not up to the plaintiff to prove fraud as an element of his or her claim." *Id.* at 24a.

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[16] Contrary to the Second Circuit's suggestion, *Lohr* does not change this analysis. *See* Pet. App. 21a-22a. The claims in *Lohr* neither arose from nor depended on federal law, whereas the claims in this case "survive[] only [if] there [is] evidence of fraud against the FDA." *Id.* 22a. Accordingly, as the *Buckman* Court explained, *Lohr* has no bearing on the preemption analysis in this case. *See* 531 U.S. at 352 (concluding that *Lohr* is an express preemption case that "did not squarely address the question of implied pre-emption" at issue in a fraud-on-the-agency inquiry).

1. The Second Circuit failed to articulate how these facial differences are relevant, in any way, to this Court's analysis in *Buckman*. And they are not. As shown, the driving considerations in *Buckman* were that (1) proof of fraud-on-the-agency (and the accompanying remedy) requires an impermissible intrusion into a field strictly within the purview of the agency alleged to have been defrauded, and (2) allowing lay jurors to make these findings imposes a direct conflict with and an obstacle to FDA's determinations within a carefully calibrated federal regulatory scheme. See 531 U.S. at 347-50.

These considerations do not depend on whether proof of fraud-on-the-agency is required in the first instance or only after an affirmative defense has been raised. In both circumstances, fact-finders improperly are empowered "to punish and deter fraud against the [FDA]" in spite of what FDA itself has done and the "delicate balance of statutory objectives" the agency has sought to fulfill. *Id.* at 348.[17]

2. The folly of the Second Circuit's focus on causes of action versus elements required to defeat an affirmative defense, while downplaying the federal inquiry required to prove each, is further highlighted by considering the analysis in this Court's complete preemption cases. Although a federal question inquiry is not at issue here, the complete preemption

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[17] *See also, e.g., In re Bextra & Celebrex Mktg. Sales Pracs. & Prod. Liab. Litig.*, MDL-1699, 2006 WL 2374742, at *10 (N.D. Cal. Aug. 16, 2006) ("a claim premised on a drug manufacturer's failure to provide data to the FDA is preempted"); Pet. App. 328a-329a (*Ledbetter v. Merck & Co.*, No. 2005-58543 (Tex. Dist. Ct. Apr. 20, 2007) ("Whether it is an element of plaintiffs' cause of action, or a way to defeat an affirmative defense, the proof is the same" and "permitting a [State] jury or judge to make the [*Buckman*] inquiry would impinge on a uniquely federal issue")).

doctrine provides a useful point of comparison. It makes plain that where federal issues are substantial and intertwined with state law, it is immaterial whether they are part of the cause of action or their resolution is simply necessary to the case's ultimate resolution. See, *e.g.*, *Smith* v. *Kansas City Title & Trust Co.*, 255 U.S. 180, 199 (1921) (discussing "right to relief depend[ing] upon the construction or application of the Constitution or laws of the United States").

Extrapolating from this Court's complete preemption principles, irrespective of whether the fraud-on-the-FDA inquiry is taken as an element of a state claim or a showing required of a plaintiff to overcome an affirmative defense, the federal issues here are so closely interwoven with the state claims that the resolution of the latter necessarily depends on determination of the former. No matter how postured, assessing whether a defendant violated a duty created by *federal* statute or regulation and owed to a *federal* agency and, if so, what action the *federal* agency with exclusive enforcement power should take are "subjects within the purview of the constitution" akin to those which trigger "the importance, and even necessity of *uniformity* of decisions throughout the whole United States." *Martin* v. *Hunter's Lessee*, 14 U.S. (1 Wheat.) 304, 347-48 (1816); cf. *Michigan* v. *Long*, 463 U.S. 1032, 1038-40 & n.4 (1983).

Given that the Michigan provision attempts to "place[] the federal law into a context where it will operate to shape behavior," and there is a strong "possibility that the federal law will be incorrectly interpreted in the context of adjudicating the state-law claim," *Thompson*, 478 U.S. at 828 (Brennan, J., dissenting), the same implied preemption concerns

that animated the Court's decision in *Buckman* are determinative here.

* * * *

Because the Michigan provision requires the trier-of-fact to make the very same inherently federal determination held to be impermissible in *Buckman*, it is preempted by federal law.[18]

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[18] The Sixth Circuit, which includes the State of Michigan, already has determined that Michigan severability law would let stand the remainder of Mich. Comp. Laws § 600.2946(5). *See Garcia*, 385 F.3d at 966-67; *see also Duronio* v. *Merck & Co.*, No. 267003, 2006 WL 1628516, at *5 (Mich. Ct. App. June 13, 2006) (per curiam) (following *Garcia* in unpublished disposition). There is no reason for this Court or the Second Circuit below to reconsider this issue of Michigan state law. *See, e.g., Elk Grove Unified Sch. Dist.* v. *Newdow*, 542 U.S. 1, 16 (2004) ("Our custom on questions of state law ordinarily is to defer to the interpretation of the Court of Appeals for the Circuit where the State is located."); *MacGregor* v. *State Mut. Life Assur. Co.*, 315 U.S. 280, 281 (1942) (per curiam) (absent State authority, "we shall leave undisturbed the interpretation placed on purely local law by a Michigan federal judge . . . and by three circuit judges whose circuit includes Michigan."); Pet. App. 11a (Second Circuit "defer[s] conclusively to another circuit's judgment only when that court of appeals' decision addressed questions of *state* law from a state within that circuit").

CONCLUSION

For these reasons, the Second Circuit's decision should be reversed and the judgment of the district court should be restored.

Respectfully submitted,

DAVID KLINGSBERG
STEVEN GLICKSTEIN
KAYE SCHOLER LLP
425 Park Avenue
New York, N.Y. 10022
(212) 836-8000

CARTER G. PHILLIPS*
DANIEL E. TROY
REBECCA K. WOOD
EAMON P. JOYCE
QUIN M. SORENSON
SIDLEY AUSTIN LLP
1501 K Street, NW
Washington, D.C. 20005
(202) 736-8000

Counsel for Petitioners

November 21, 2007

* Counsel of Record

APPENDIX

APPENDIX A

STATUTES

21 U.S.C. § 336. Report of minor violations

Nothing in this chapter shall be construed as requiring the Secretary to report for prosecution, or for the institution of libel or injunction proceedings, minor violations of this chapter whenever he believes that the public interest will be adequately served by a suitable written notice or warning.

21 U.S.C. § 375. Publicity

* * * * *

(b) Information regarding certain goods

The Secretary may also cause to be disseminated information regarding food, drugs, devices, or cosmetics in situations involving, in the opinion of the Secretary, imminent danger to health or gross deception of the consumer. Nothing in this section shall be construed to prohibit the Secretary from collecting, reporting, and illustrating the results of the investigations of the Department.

APPENDIX B

REGULATIONS

21 C.F.R. § 20.1 Testimony by Food and Drug Administration employees.

(a) No officer or employee of the Food and Drug Administration or of any other office or establishment in the Department of Health and Human Services, except as authorized by the Commissioner of Food and Drugs pursuant to this section or in the discharge of his official duties under the laws administered by the Food and Drug Administration, shall give any testimony before any tribunal pertaining to any function of the Food and Drug Administration or with respect to any information acquired in the discharge of his official duties.

(b) Whenever a subpoena, in appropriate form, has been lawfully served upon an officer or employee of the Food and Drug Administration commanding the giving of any testimony, such officer or employee shall, unless otherwise authorized by the Commissioner, appear in response thereto and respectfully decline to testify on the grounds that it is prohibited by this section.

(c) A person who desires testimony from any employee may make written request therefor, verified by oath, directed to the Commissioner setting forth his interest in the matter sought to be disclosed and designating the use to which such testimony will be put in the event of compliance with such request: *Provided*, That a written request therefor made by a health, food, or drug officer, prosecuting attorney, or member of the judiciary of any State, Territory, or political subdivision thereof, acting in his official capacity, need not be verified by oath. If it is

determined by the Commissioner, or any other officer or employee of the Food and Drug Administration whom he may designate to act on his behalf for the purpose, that such testimony will be in the public interest and will promote the objectives of the act and the agency, the request may be granted. Where a request for testimony is granted, one or more employees of the Food and Drug Administration may be designated to appear, in response to a subpoena, and testify with respect thereto.

21 C.F.R. § 314.125 Refusal to approve an application.

(a) The Food and Drug Administration will refuse to approve the application and for a new drug give the applicant written notice of an opportunity for a hearing under § 314.200 on the question of whether there are grounds for denying approval of the application under section 505(d) of the act, if:

(1) FDA sends the applicant an approvable or a not approvable letter under § 314.110 or § 314.120;

(2) The applicant requests an opportunity for hearing for a new drug on the question of whether the application is approvable; and

(3) FDA finds that any of the reasons given in paragraph (b) of this section apply.

(b) FDA may refuse to approve an application for any of the following reasons:

(1) The methods to be used in, and the facilities and controls used for, the manufacture, processing, packing, or holding of the drug substance or the drug product are inadequate to preserve its

identity, strength, quality, purity, stability, and bioavailability.

(2) The investigations required under section 505(b) of the act do not include adequate tests by all methods reasonably applicable to show whether or not the drug is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling.

(3) The results of the tests show that the drug is unsafe for use under the conditions prescribed, recommended, or suggested in its proposed labeling or the results do not show that the drug product is safe for use under those conditions.

(4) There is insufficient information about the drug to determine whether the product is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling.

(5) There is a lack of substantial evidence consisting of adequate and well-controlled investigations, as defined in § 314.126, that the drug product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in its proposed labeling.

(6) The proposed labeling is false or misleading in any particular.

(7) The application contains an untrue statement of a material fact.

(8) The drug product's proposed labeling does not comply with the requirements for labels and labeling in Part 201.

(9) The application does not contain bioavailability or bioequivalence data required under

part 320 of this chapter.

(10) A reason given in a letter refusing to file the application under § 314.101(d), if the deficiency is not corrected.

(11) The drug will be manufactured or processed in whole or in part in an establishment that is not registered and not exempt from registration under section 510 of the act and Part 207.

(12) The applicant does not permit a properly authorized officer or employee of the Department of Health and Human Services an adequate opportunity to inspect the facilities, controls, and any records relevant to the application.

(13) The methods to be used in, and the facilities and controls used for, the manufacture, processing, packing, or holding of the drug substance or the drug product do not comply with the current good manufacturing practice regulations in Parts 210 and 211.

(14) The application does not contain an explanation of the omission of a report of any investigation of the drug product sponsored by the applicant, or an explanation of the omission of other information about the drug pertinent to an evaluation of the application that is received or otherwise obtained by the applicant from any source.

(15) A nonclinical laboratory study that is described in the application and that is essential to show that the drug is safe for use under the conditions prescribed, recommended, or suggested in its proposed labeling was not conducted in compliance with the good laboratory practice regulations in part 58 of this chapter and no

reason for the noncompliance is provided or, if it is, the differences between the practices used in conducting the study and the good laboratory practice regulations do not support the validity of the study.

(16) Any clinical investigation involving human subjects described in the application, subject to the institutional review board regulations in part 58 of this chapter or informed consent regulations in part 50 of this chapter, was not conducted in compliance with those regulations such that the rights or safety of human subjects were not adequately protected.

(17) The applicant or contract research organization that conducted a bioavailability or bioequivalence study described in § 320.38 or § 320.63 of this chapter that is contained in the application refuses to permit an inspection of facilities or records relevant to the study by a properly authorized officer or employee of the Department of Health and Human Services or refuses to submit reserve samples of the drug products used in the study when requested by FDA.

(18) For a new drug, the application failed to contain the patent information required by section 505(b)(1) of the act.

(c) For drugs intended to treat life-threatening or severely-debilitating illnesses that are developed in accordance with §§ 312.80 through 312.88 of this chapter, the criteria contained in paragraphs (b) (3), (4), and (5) of this section shall be applied according to the considerations contained in § 312.84 of this chapter.